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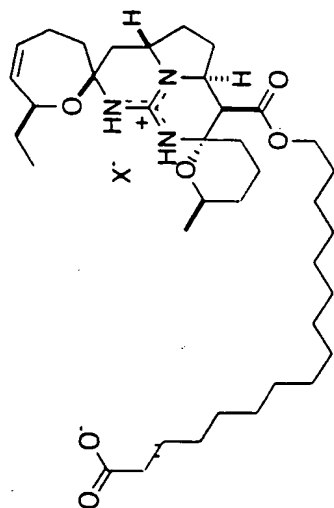
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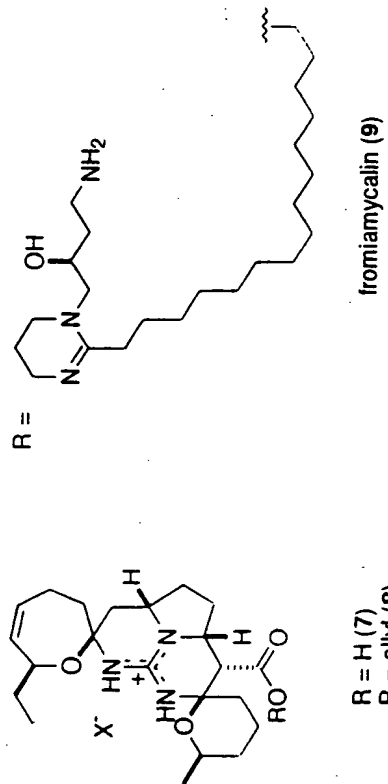
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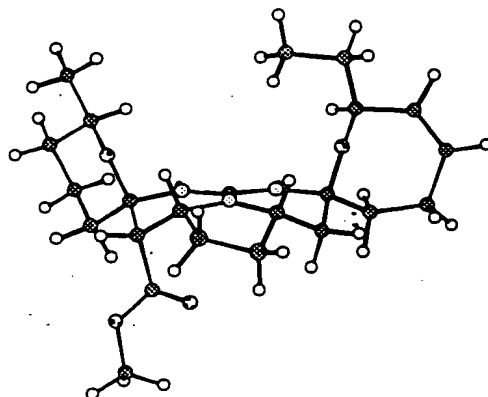
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**13, 14, 15 - isocrambescidin 657 (10a)**



### Figure 1



**Figure 2**

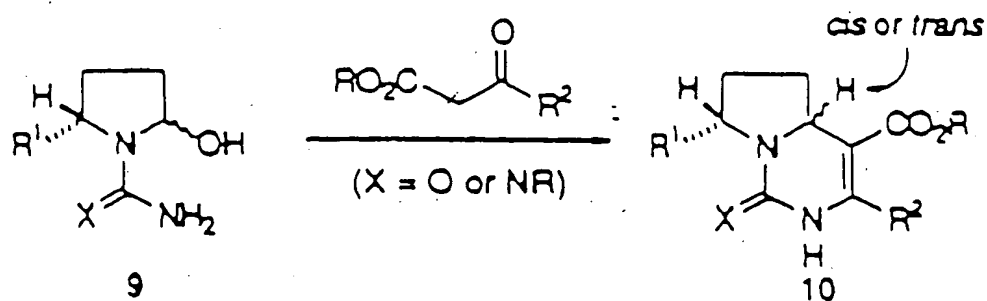
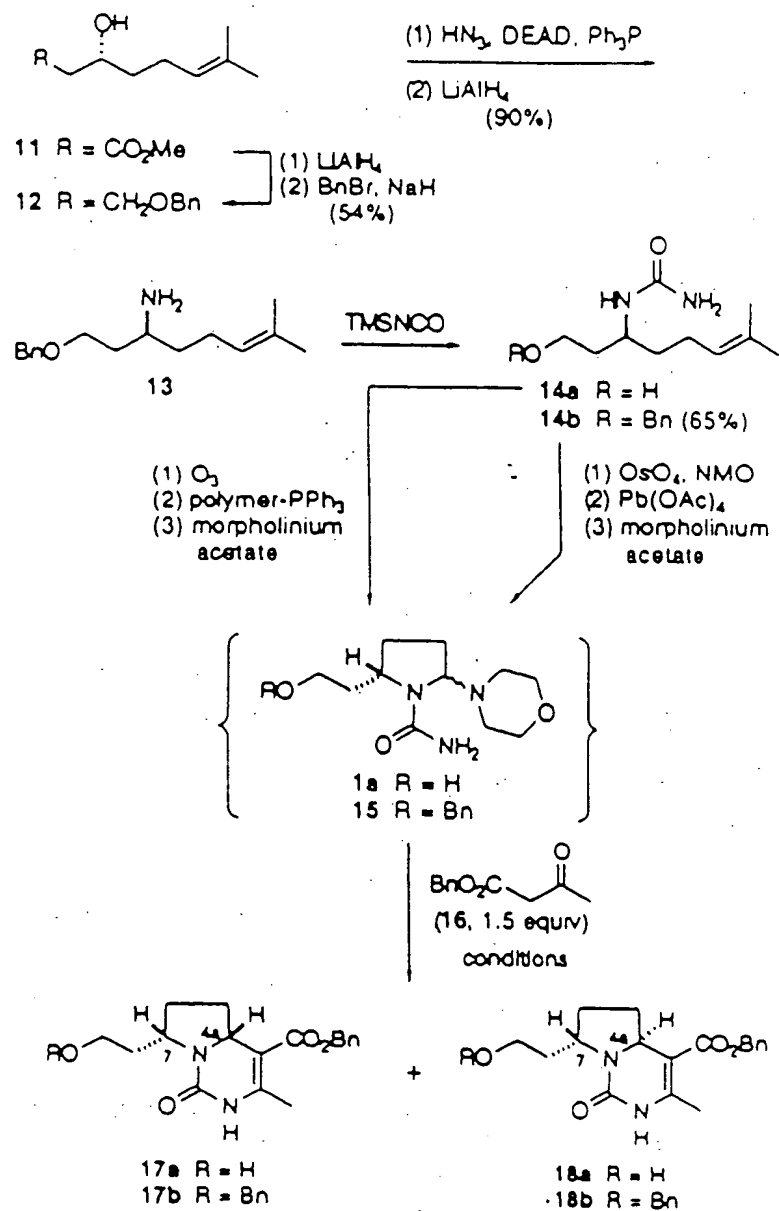


FIGURE .3



substrate	reaction conditions	17:18 (yield) <sup>a</sup>
1a	morpholinium acetate (1.5 eq),	4:1 (80%)
15	$\text{CF}_3\text{CH}_2\text{OH}$ , 60 °C, 48 h	4:1 (81%)
15	PPE, $\text{CH}_2\text{Cl}_2$ , 23 °C, 48 h	1:4 (60%)

<sup>a</sup> Combined overall yield of 17 and 18 from 14.

FIGURE 4

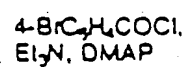
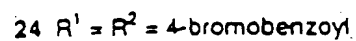
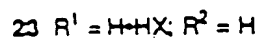
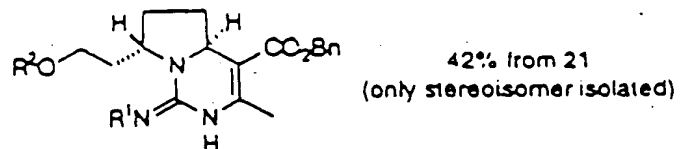
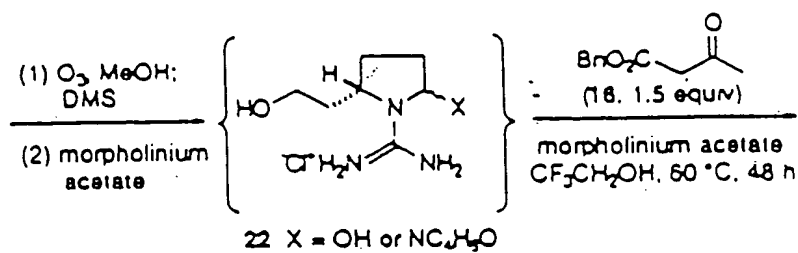
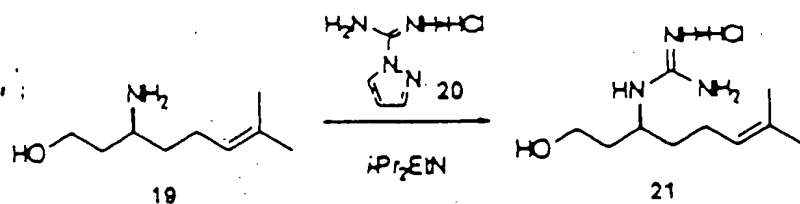
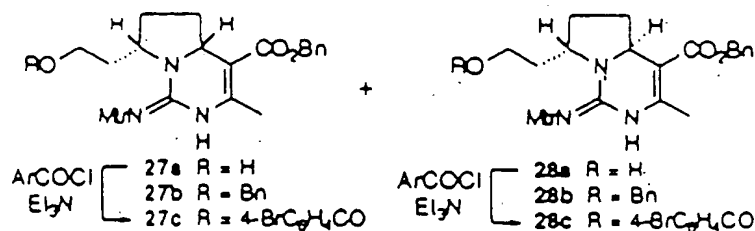
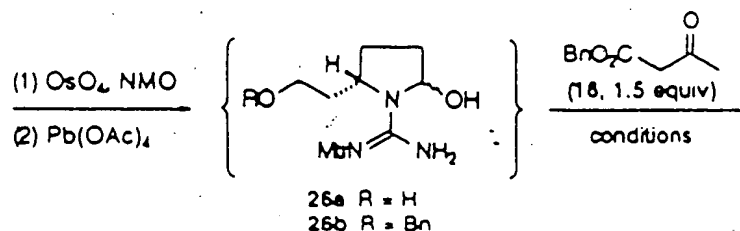
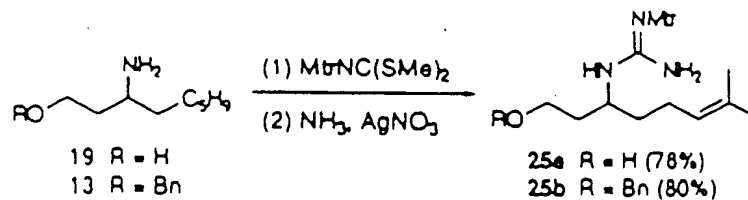


FIGURE 5



substrate	reaction conditions	27:28 (yield) <sup>a</sup>
26a	morpholinium acetate (1.5 eq),	6:1 (61%)
26b	CF <sub>3</sub> CH <sub>2</sub> OH, 60 °C, 48 h	7:1 (84%)
26b	PPE, CH <sub>2</sub> Cl <sub>2</sub> , 23 °C, 48 h	1:20 (61%)

<sup>a</sup> Combined overall yield of 27 and 28 from 25.

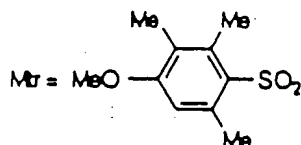


FIGURE 6

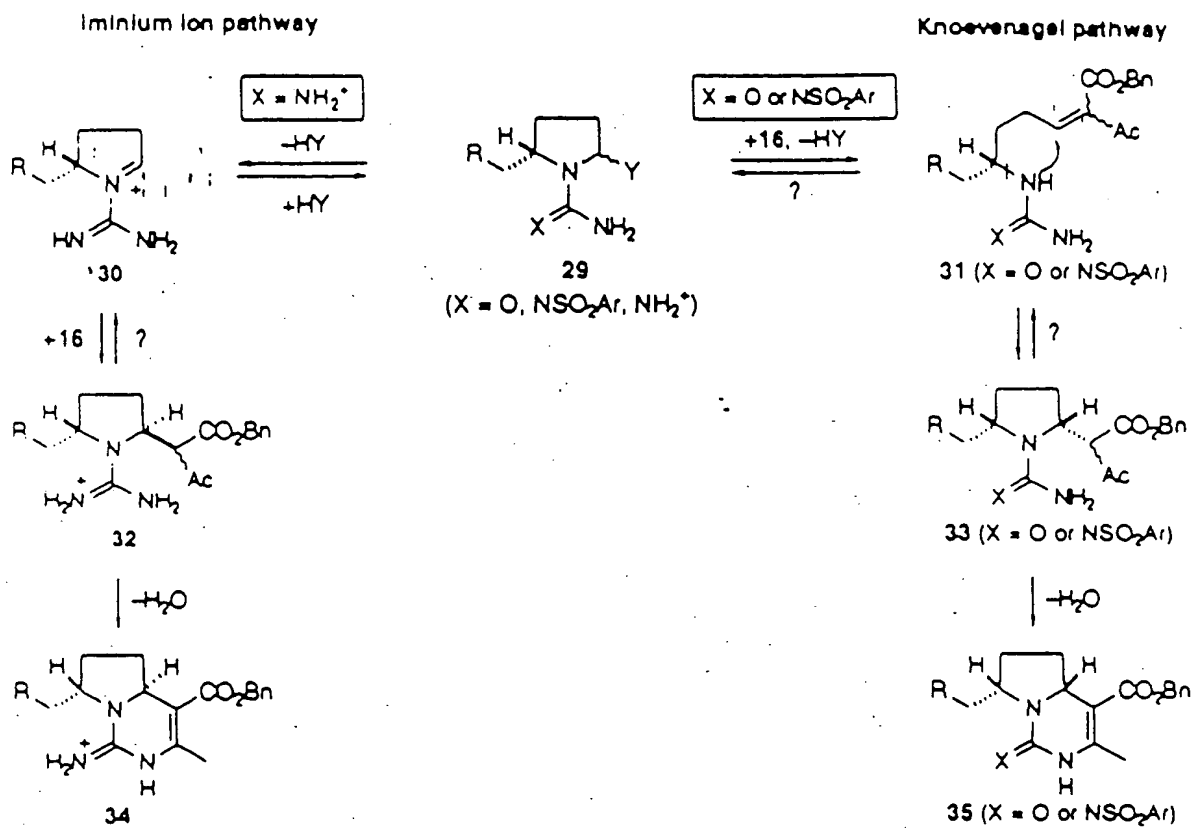


FIGURE 7



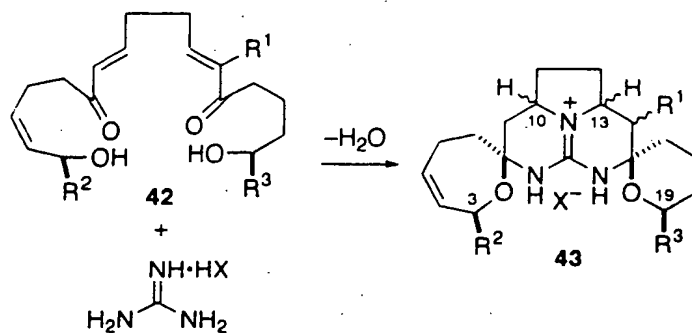
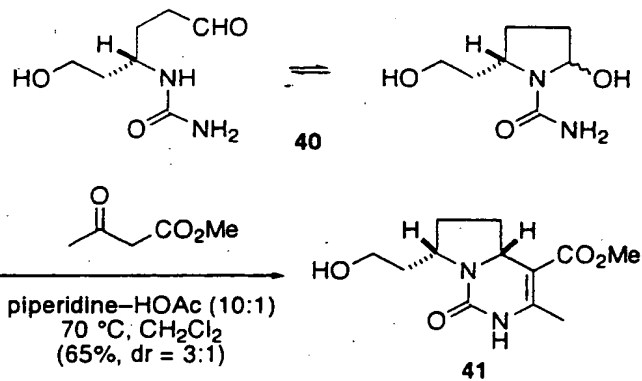
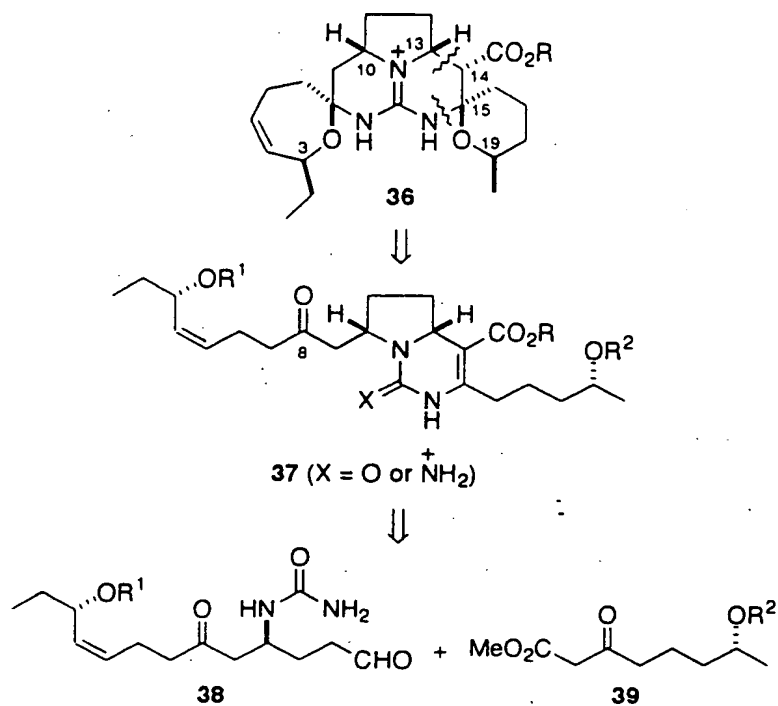
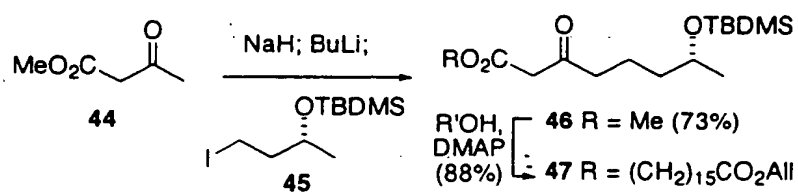
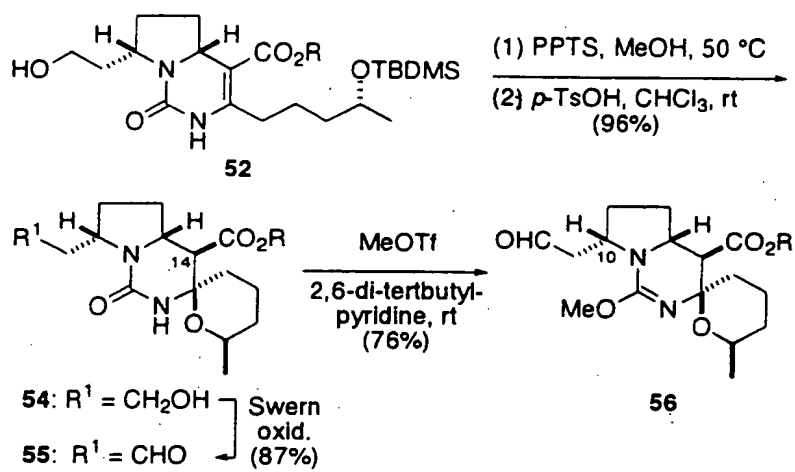


Figure 8

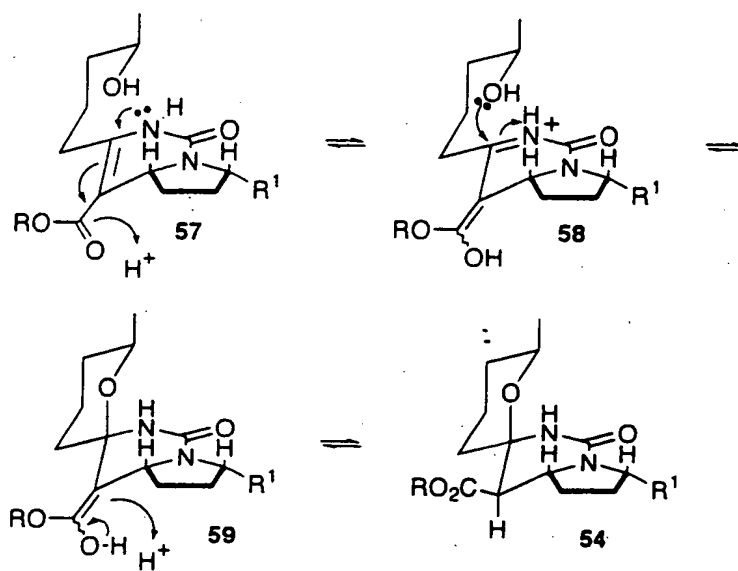


**Figure 9**





**Figure 11**



**Figure 12**

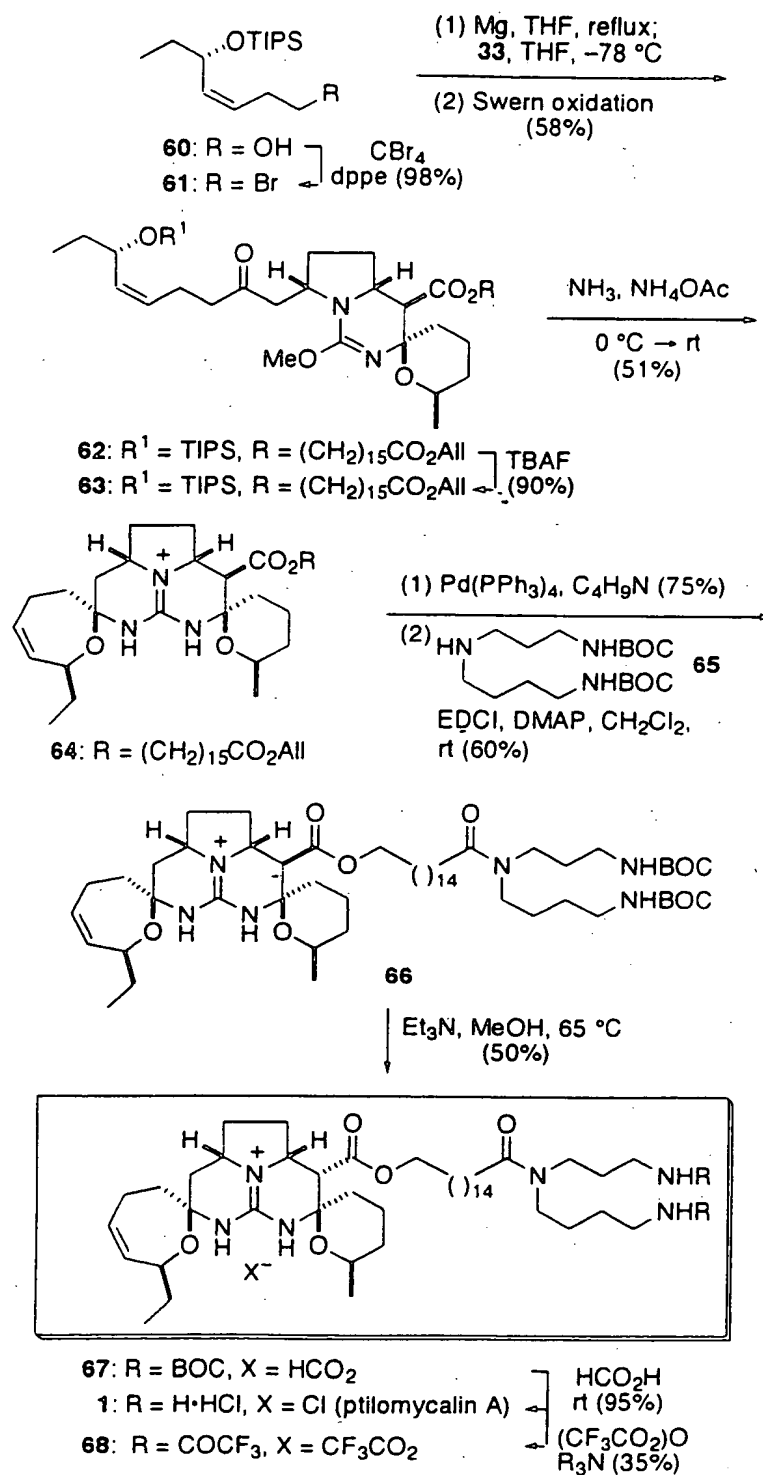
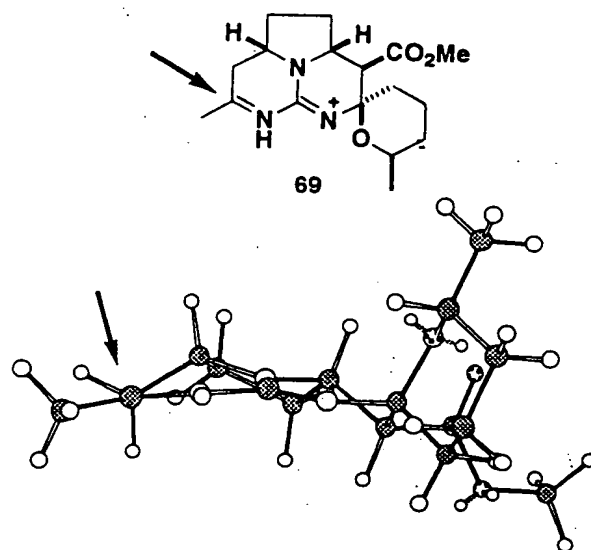


Figure 13



**Figure 14**

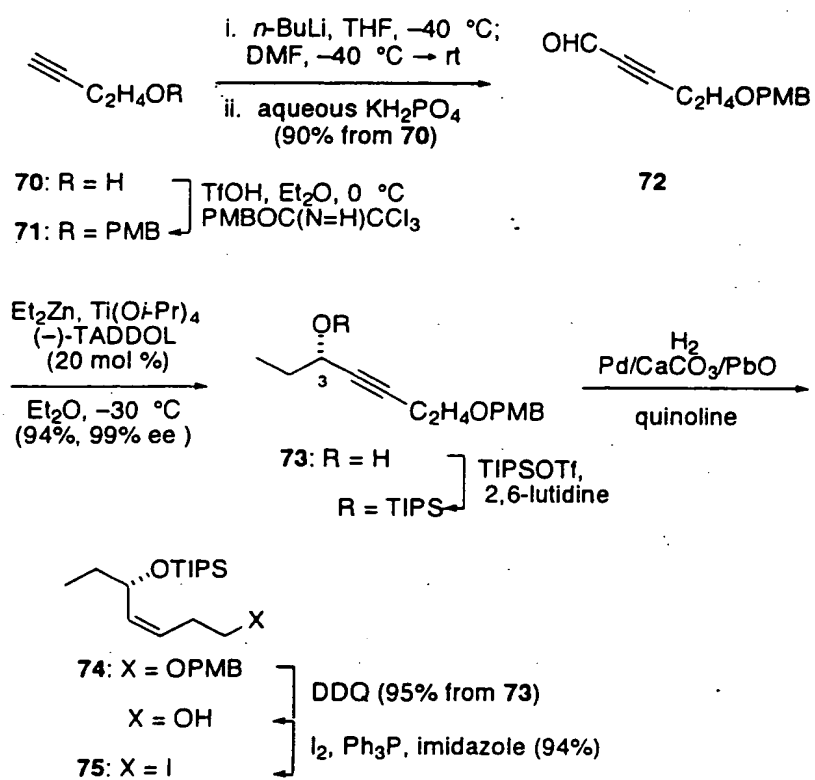


Figure 15





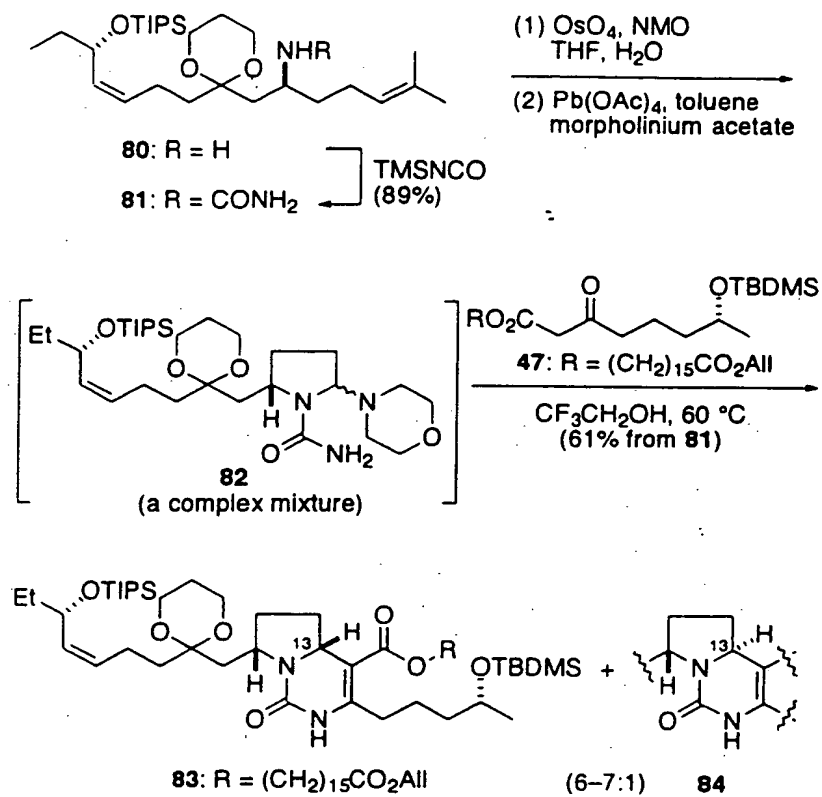
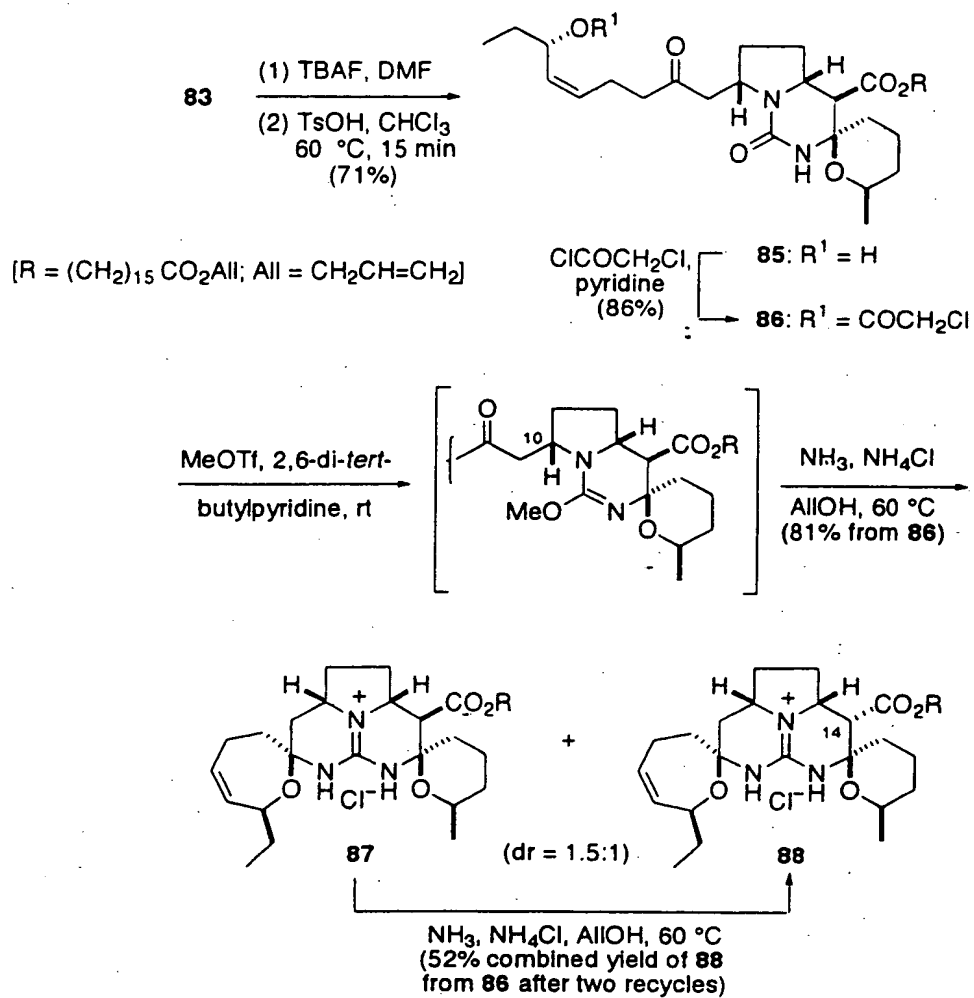


Figure 17



**Figure 18**

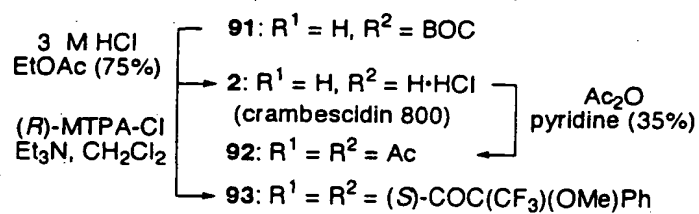
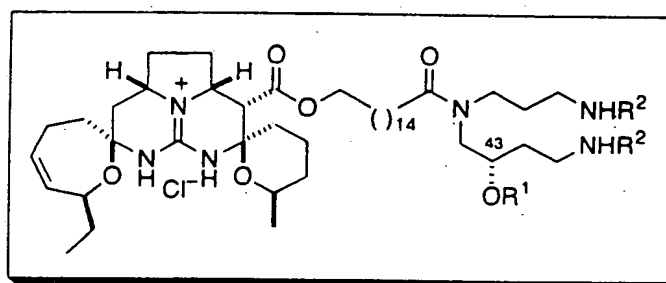
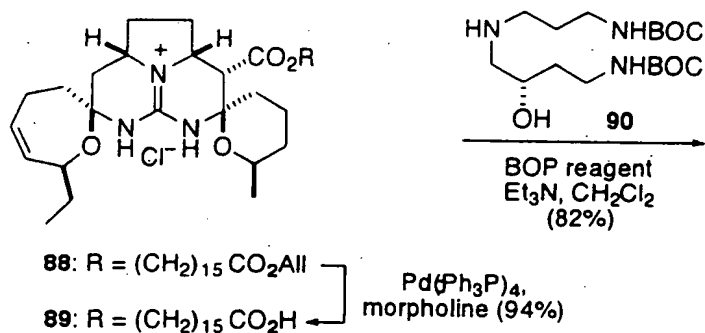
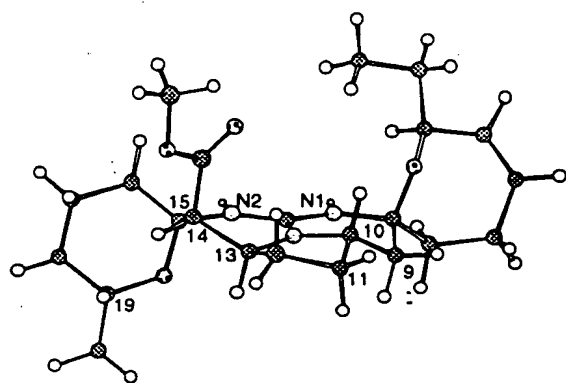
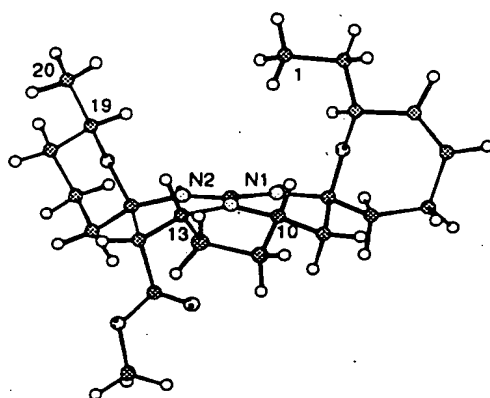


Figure 19

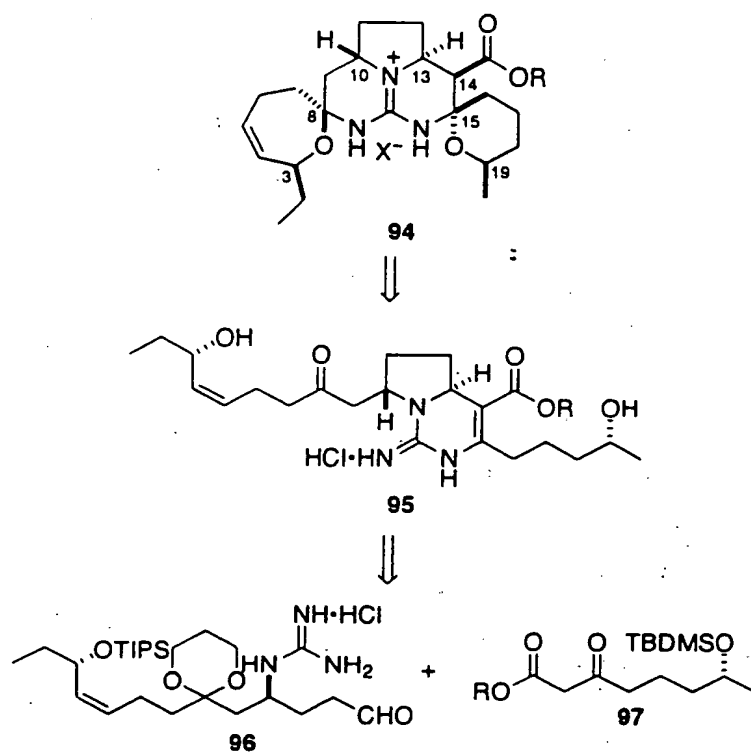


13,14,15-isocrambescidin core



crambescidin/ptilomycalin A core

**Figure 20**



**Figure 21**

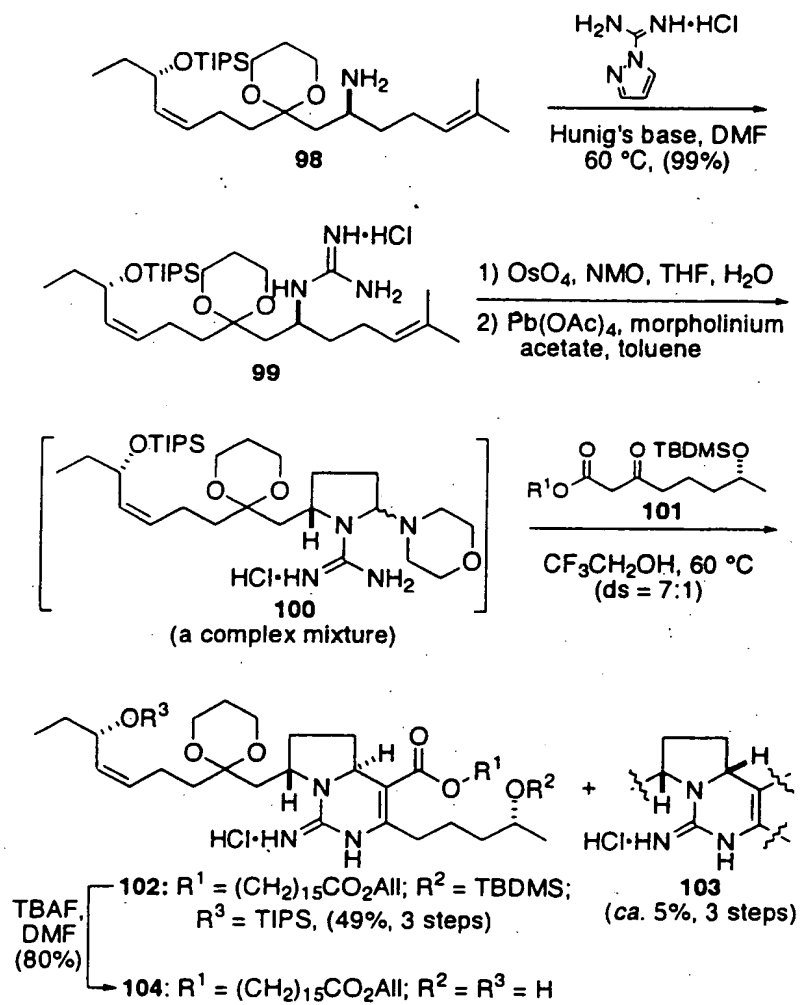
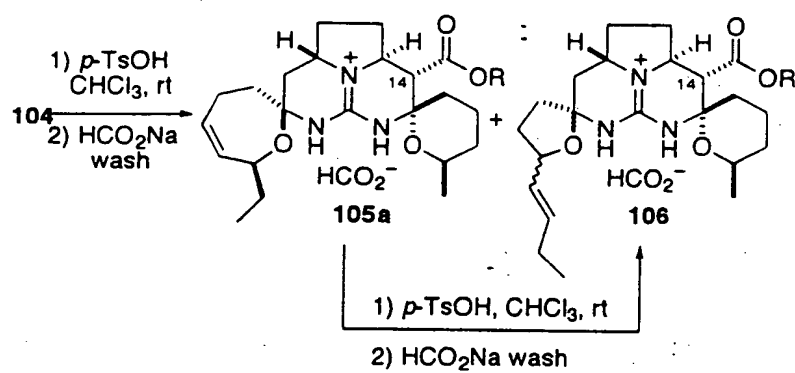


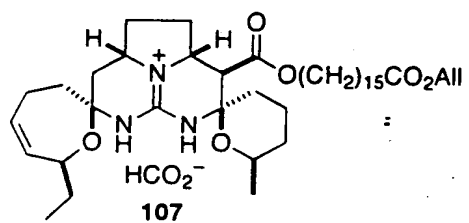
Figure 22

$R = (CH_2)_{15}CO_2AlI$



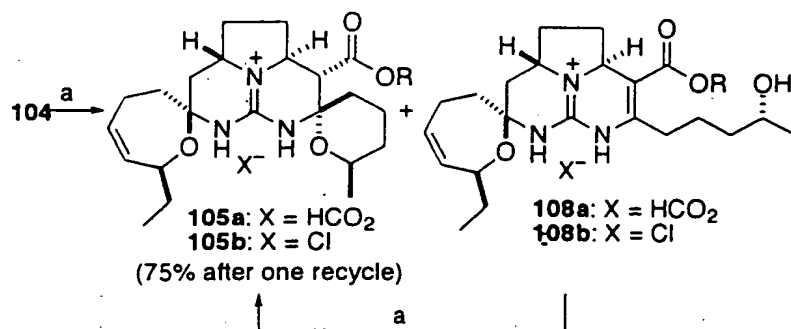
**Figure 23**





**Figure 24**

$R = (CH_2)_{15}CO_2AlI$



<sup>a</sup>Reagents: (a) PPTS,  $CHCl_3$ , 90 °C, 24 h;  $HCO_2 Na$  wash or 0.1 N HCl wash

Figure 25

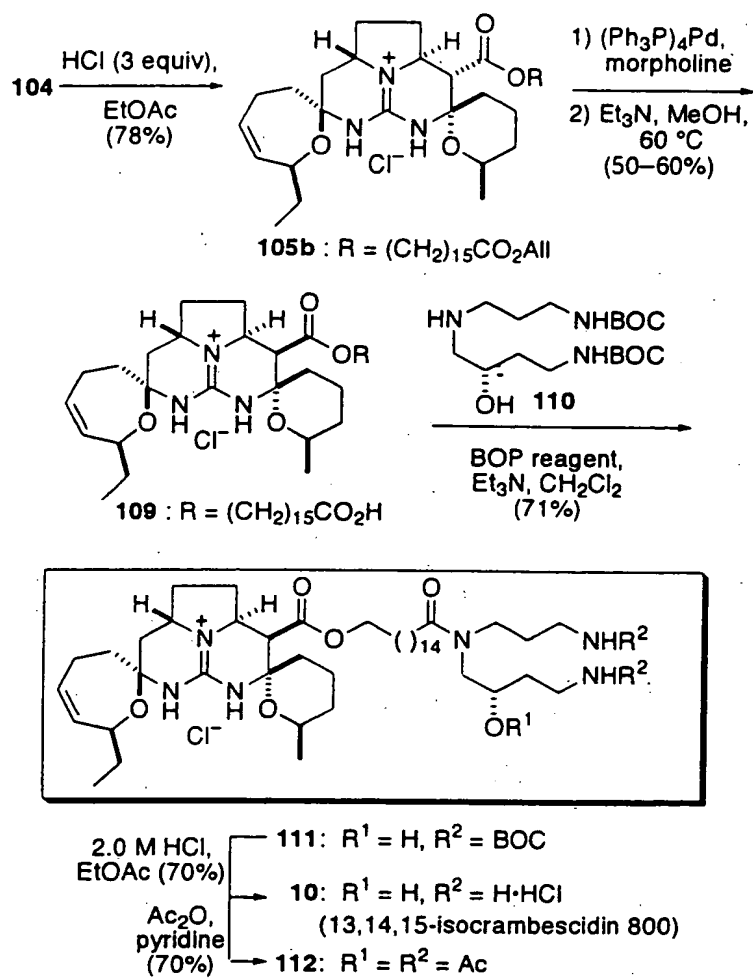
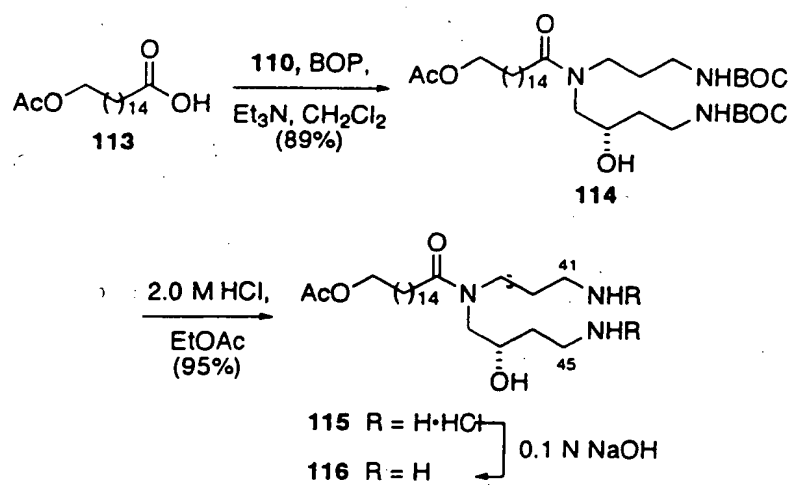
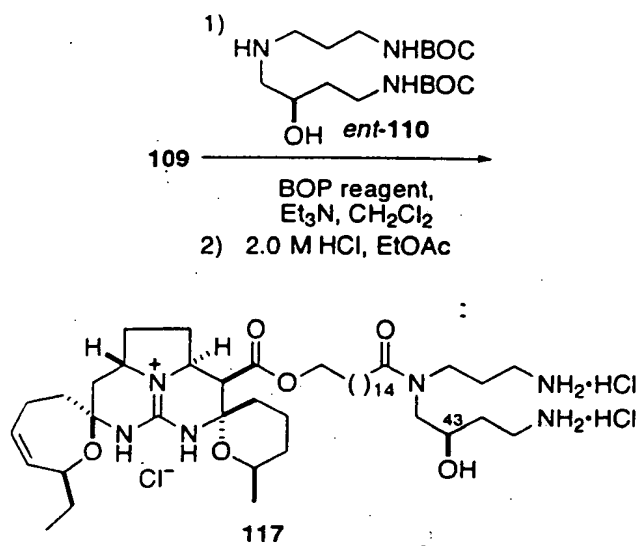


Figure 26



**Figure 27**

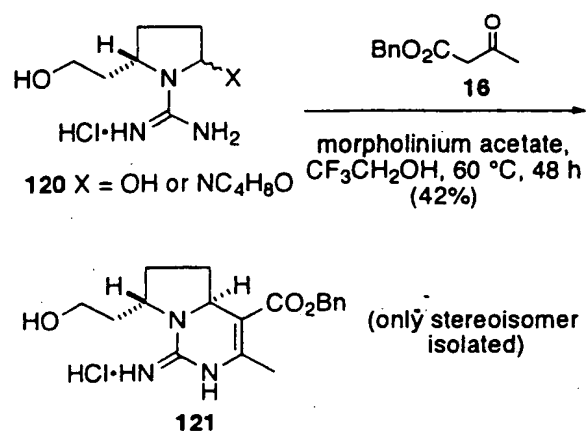


**Figure 28**

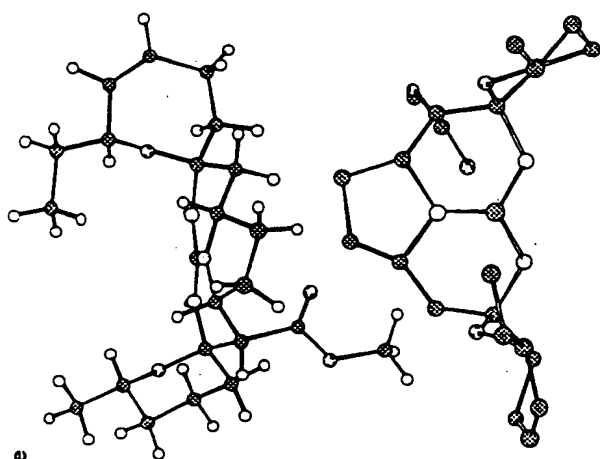
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		<div> <div>118 : 43S</div> <div>119 : 43R</div> </div>	
entry	starting material	product	<sup>19</sup> F NMR (CDCl <sub>3</sub> ) <sup>a</sup> , δ ppm
1	synthetic 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	117	119	-68.6, -68.7, -68.8, -68.9, -71.0, -71.1
3	natural 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

<sup>a</sup>Due to rotamers about the C38 amide, there are six peaks in the <sup>19</sup>F NMR spectra.

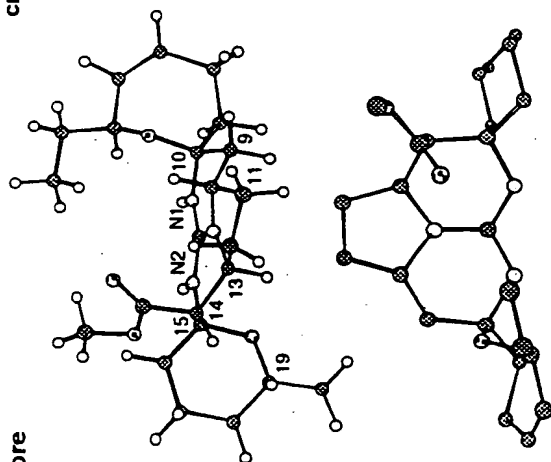
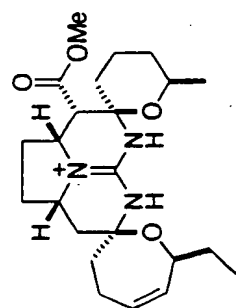
Figure 29



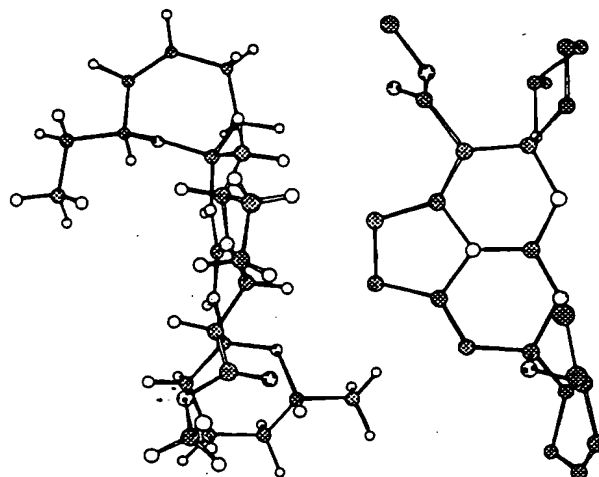
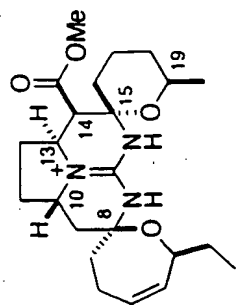
**Figure 30**



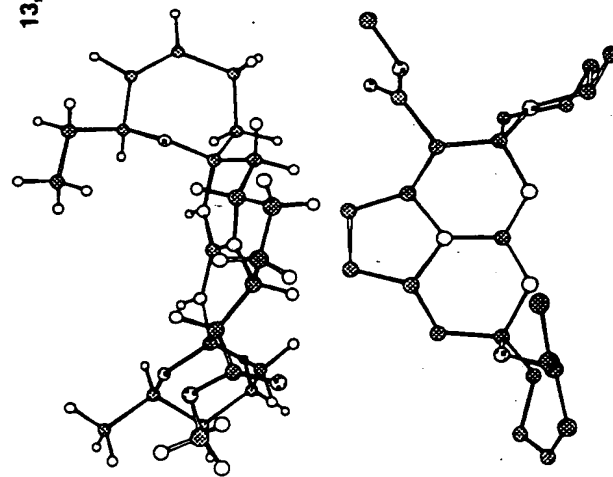
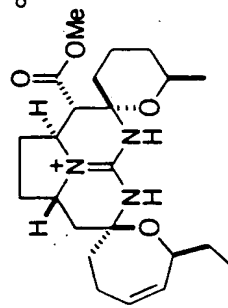
crambescidin/ptilomycalin A core



13,14,15-isocrambescidin core



13,15-epicrambescidin core



13-epicrambescidin core

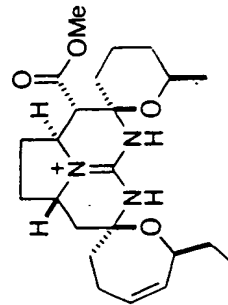
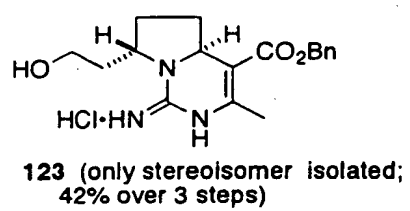
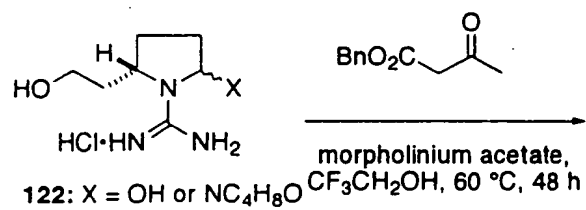
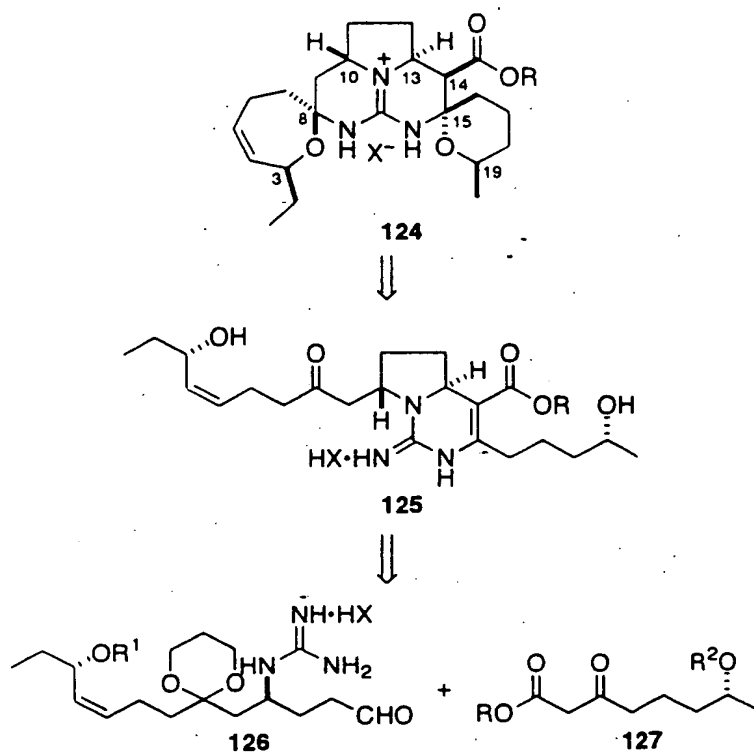


Figure 31





**Figure 32**



**Figure 33**

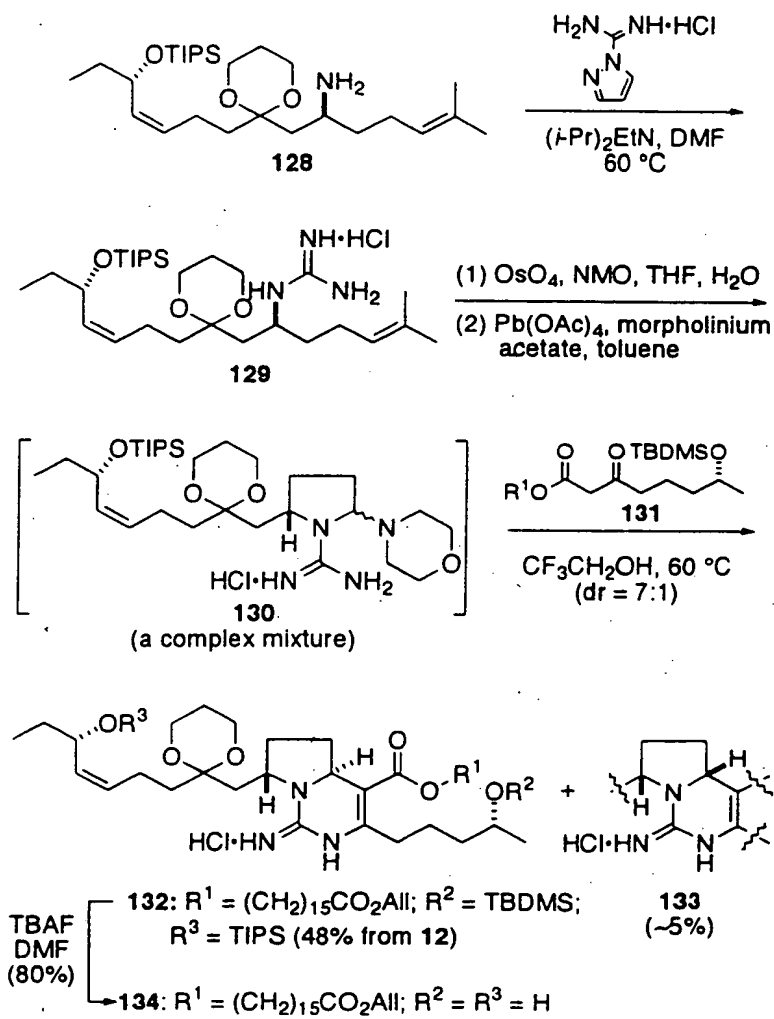
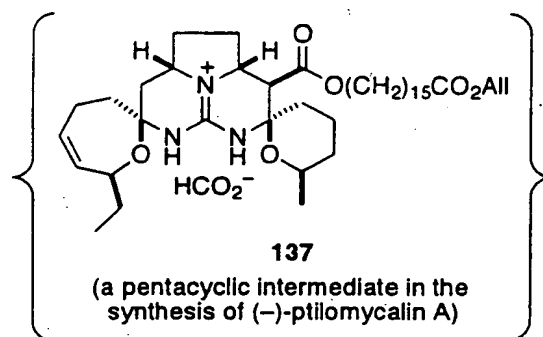
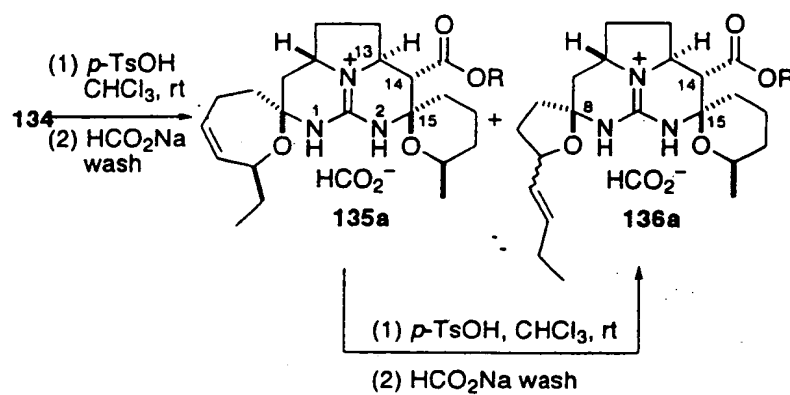


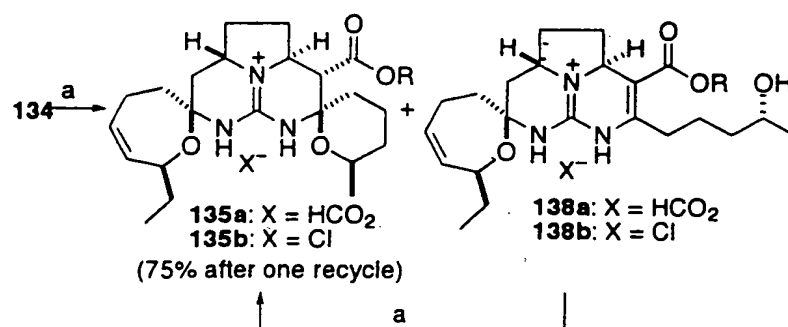
Figure 34

$R = (CH_2)_{15}CO_2All$



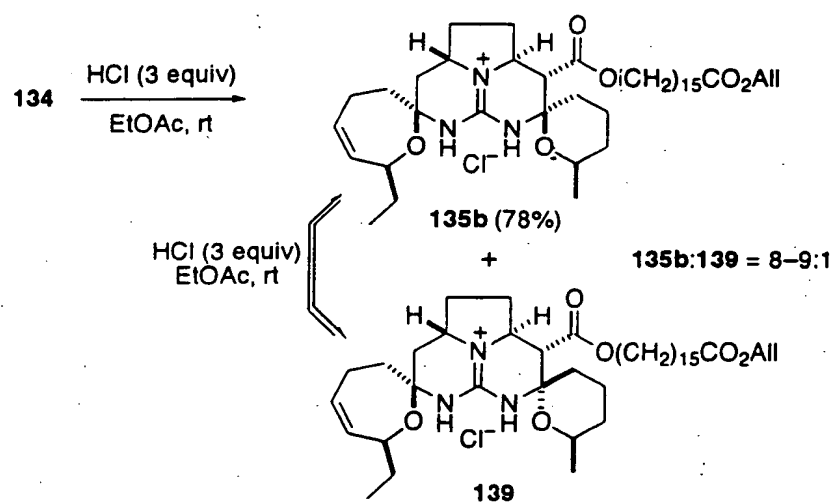
**Figure 35**

$R = (CH_2)_{15}CO_2AlI$



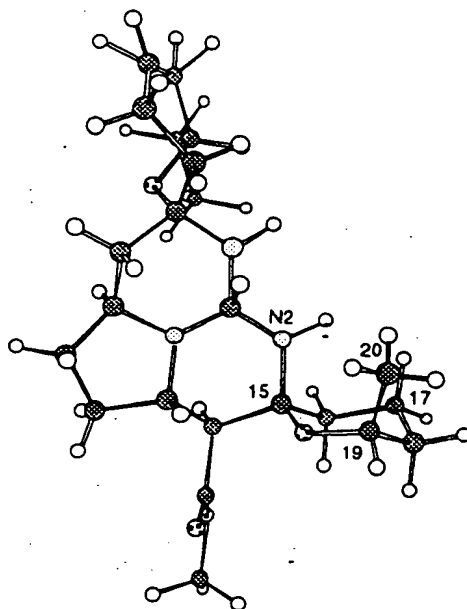
<sup>a</sup>Reagents: (a) PPTS,  $CHCl_3$ , 90 °C, 24 h;  $HCO_2Na$  wash or 0.1 N HCl wash

Figure 36

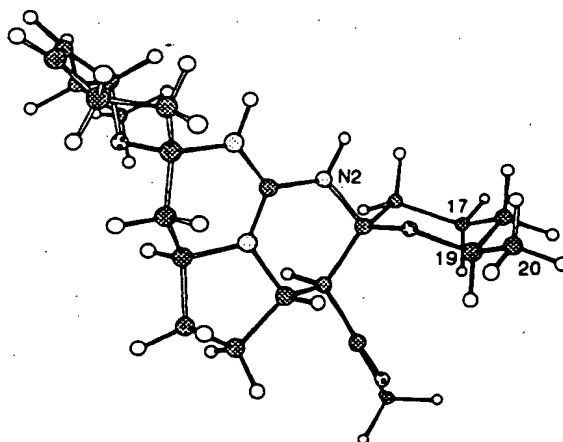


**Figure 37**

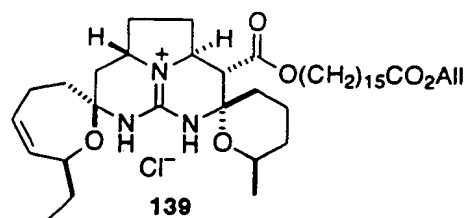
**A**



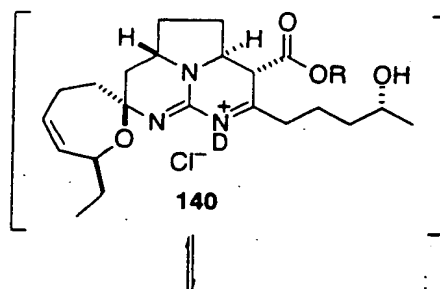
**B**



**Figure 38**



DCI, EtOAc  
rt, 24 h



no deuterium  
incorporation  
at C14

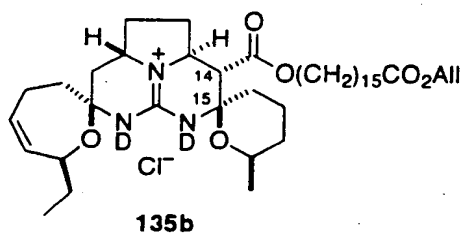
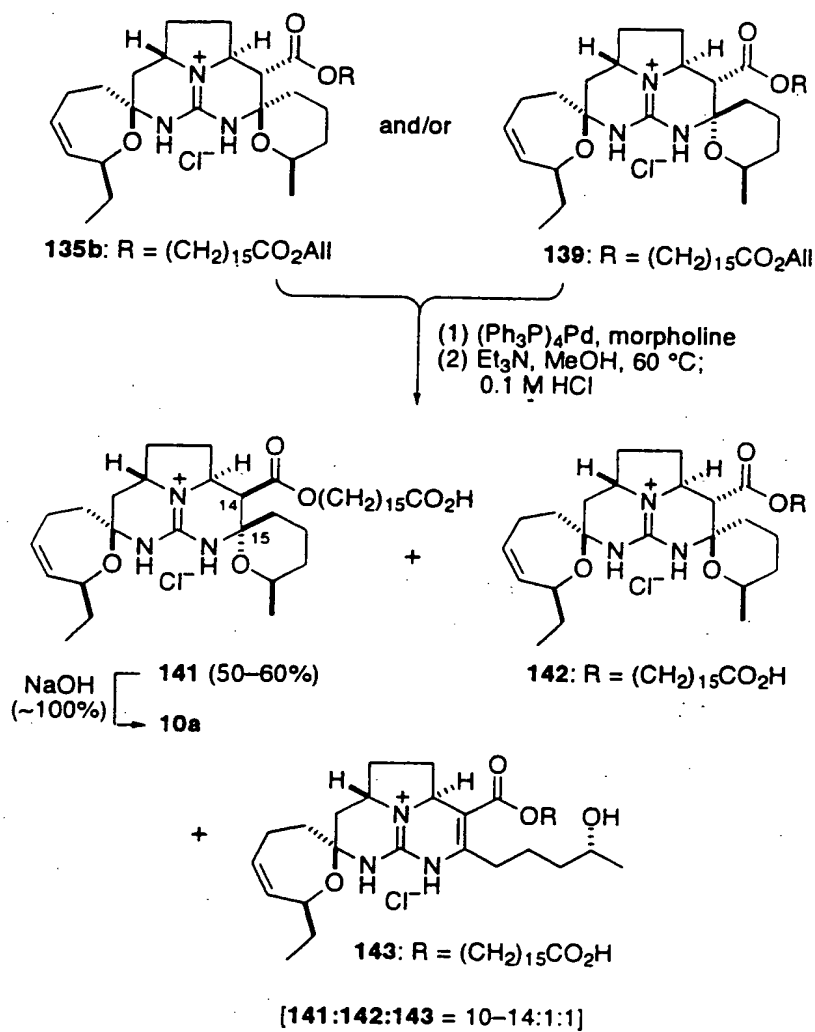
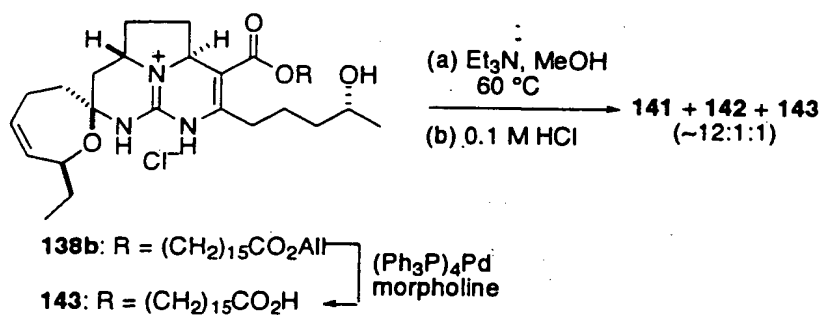


Figure 39





**Figure 40**



**Figure 41**

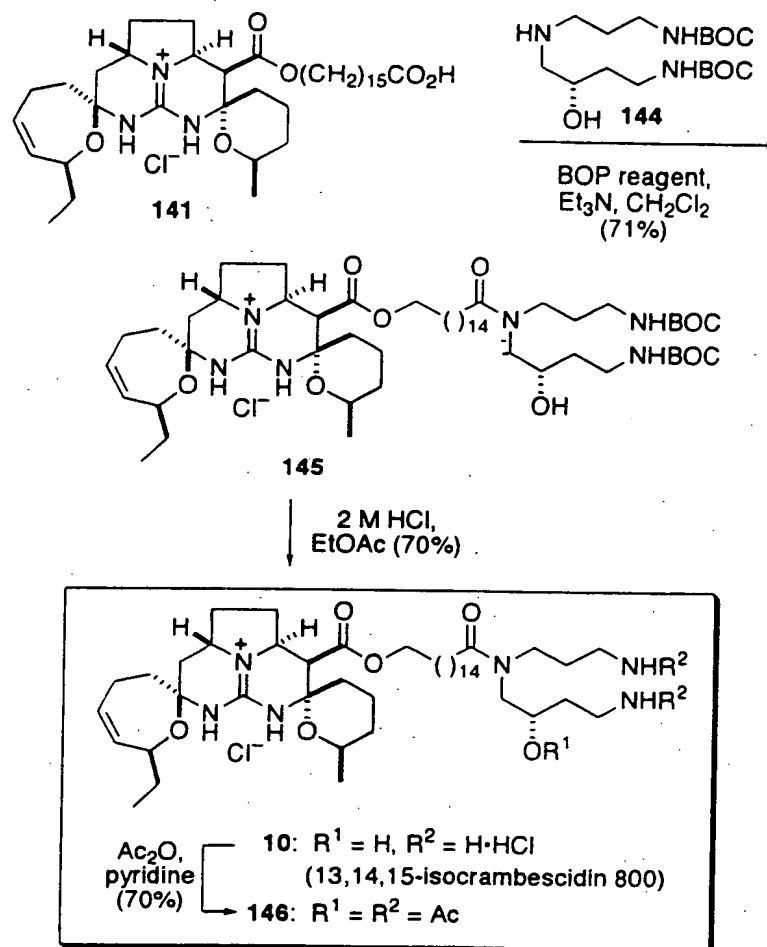
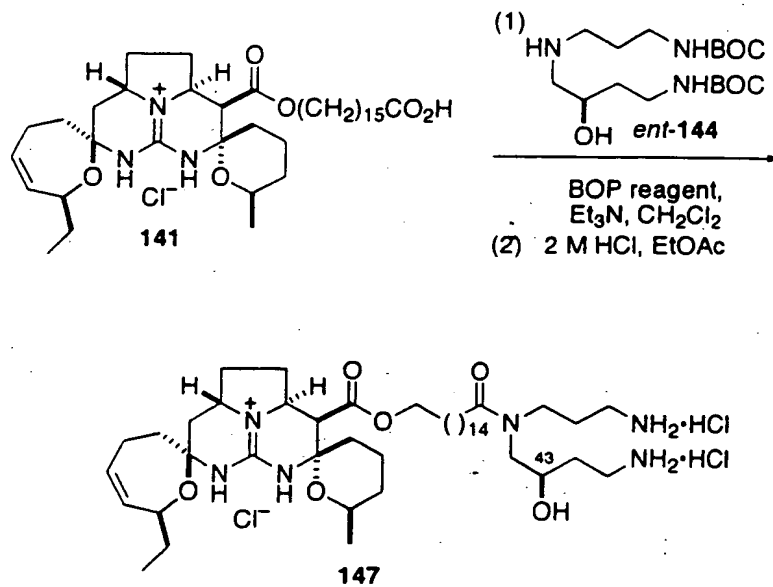
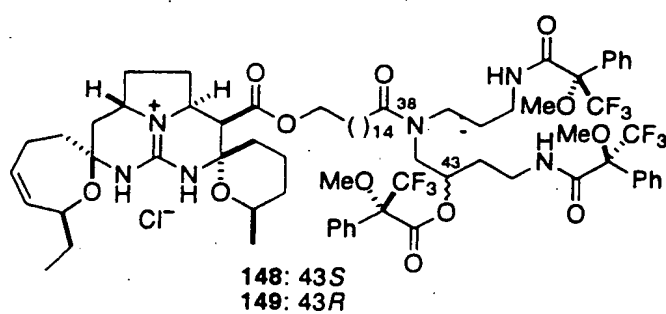


Figure 42



**Figure 43**



entry	starting material	product	$^{19}\text{F}$ NMR ( $\text{CDCl}_3$ ) <sup>a</sup> , $\delta$ ppm
1	synthetic 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	147	149	-68.6, -68.7, -68.8, -68.9, -71.0, -71.1
3	natural 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

<sup>a</sup>Due to rotamers about the C38 amide bond on the NMR time scale, six peaks are observed in the  $^{19}\text{F}$  NMR spectra.

**Figure 44**

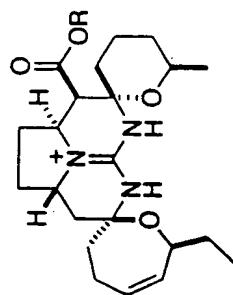
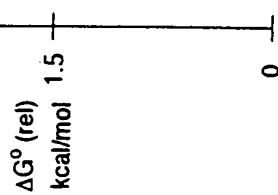
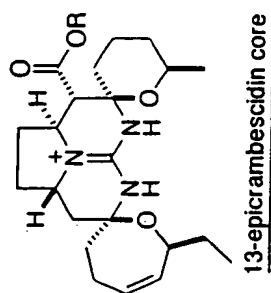
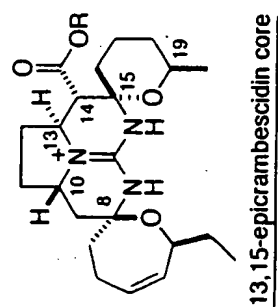


Figure 45

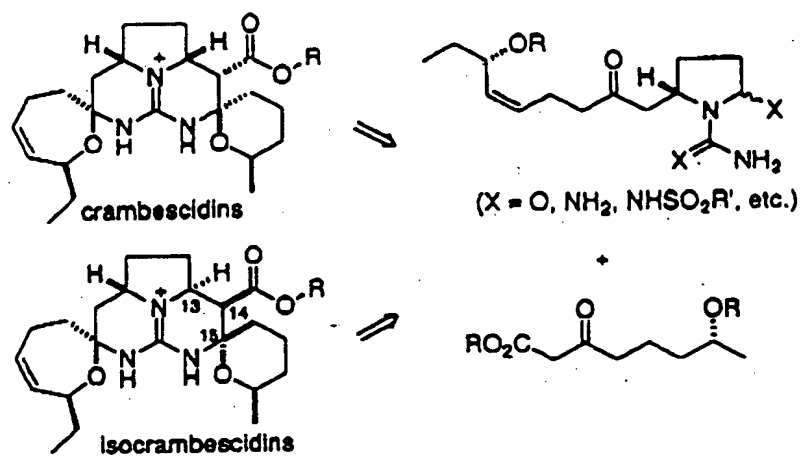
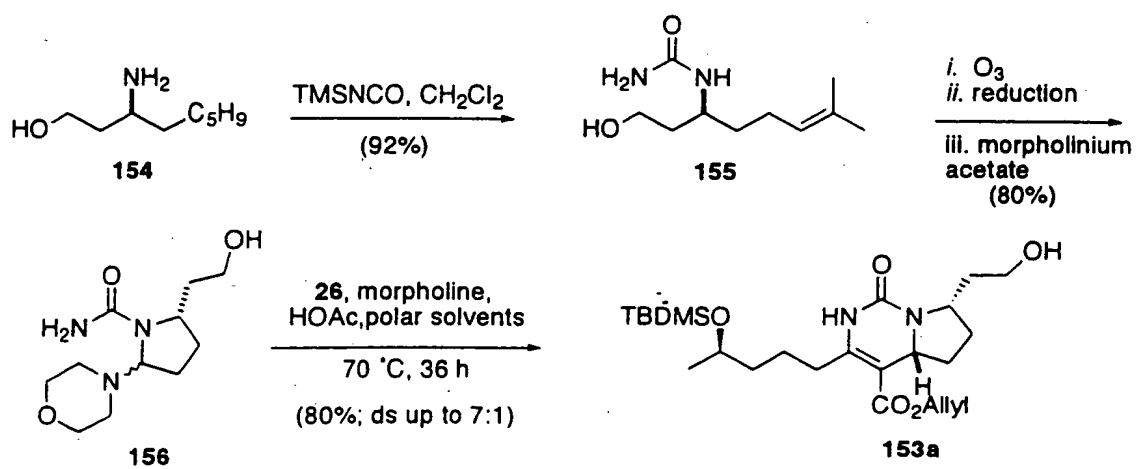


Figure 46







**Figure 48**



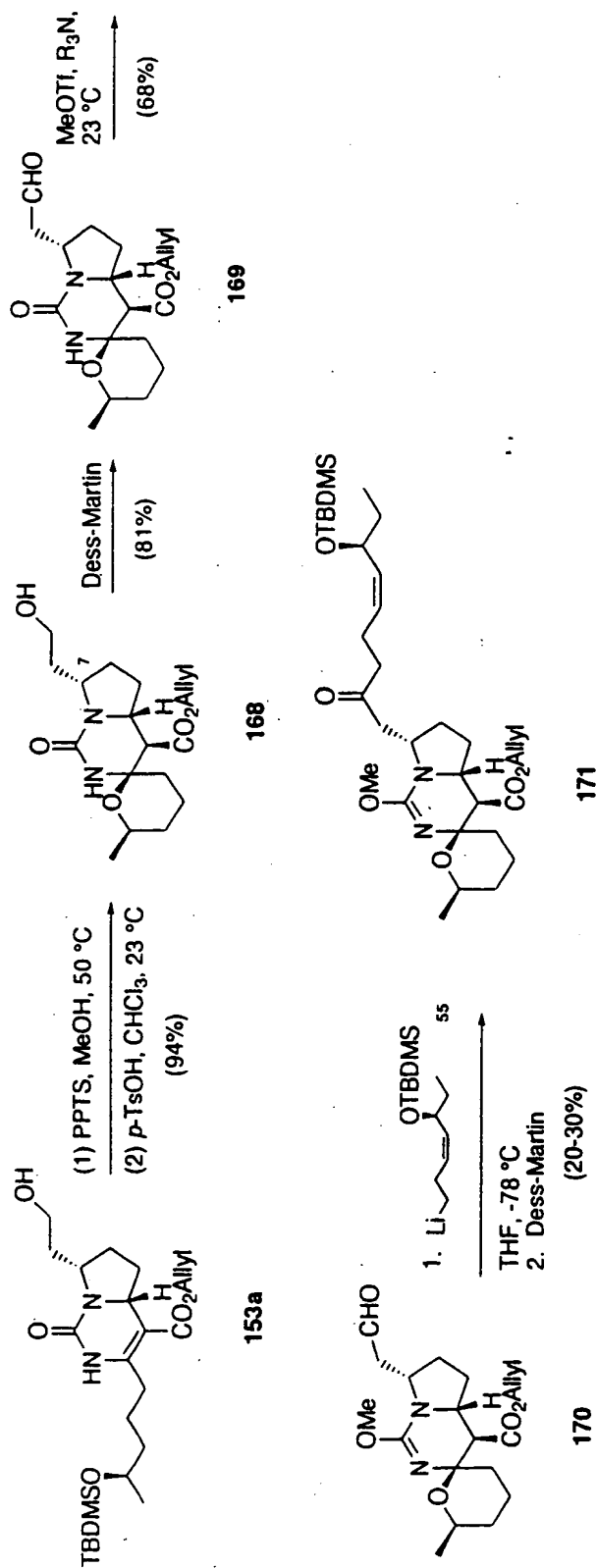
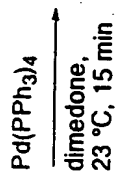
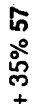


Figure 50



**Figure 51**

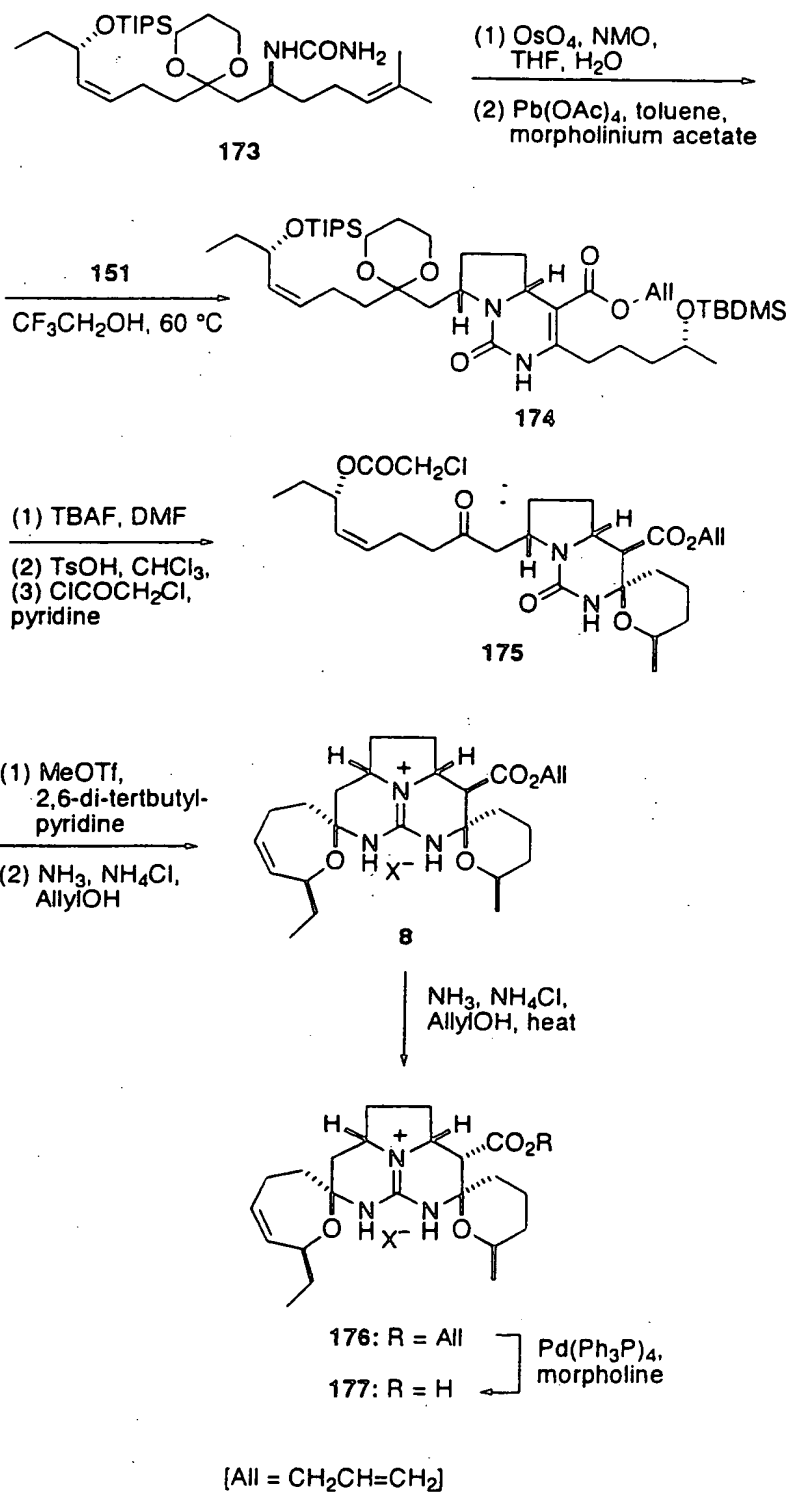


Figure 52

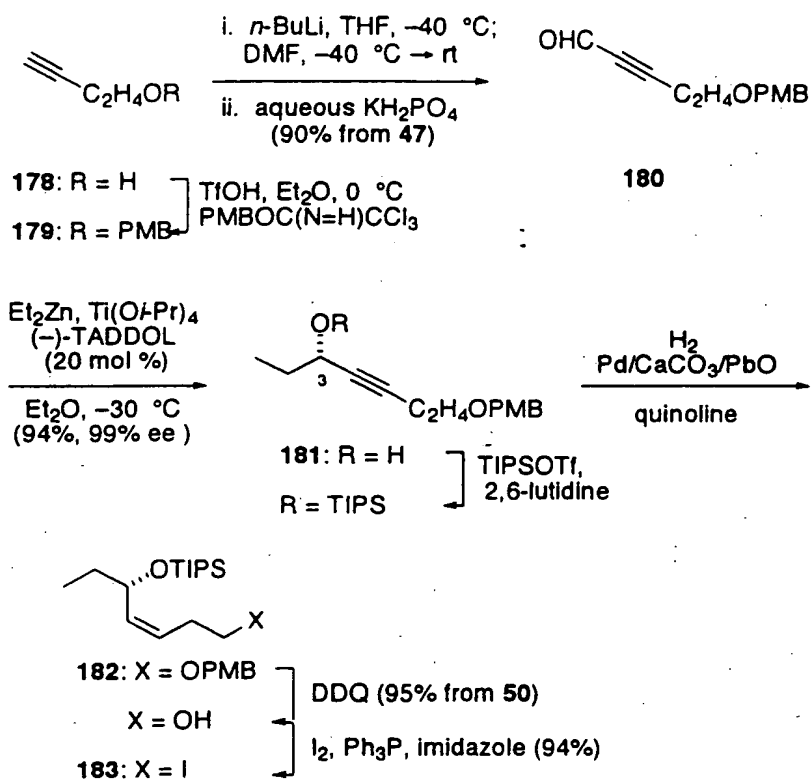


Figure 53

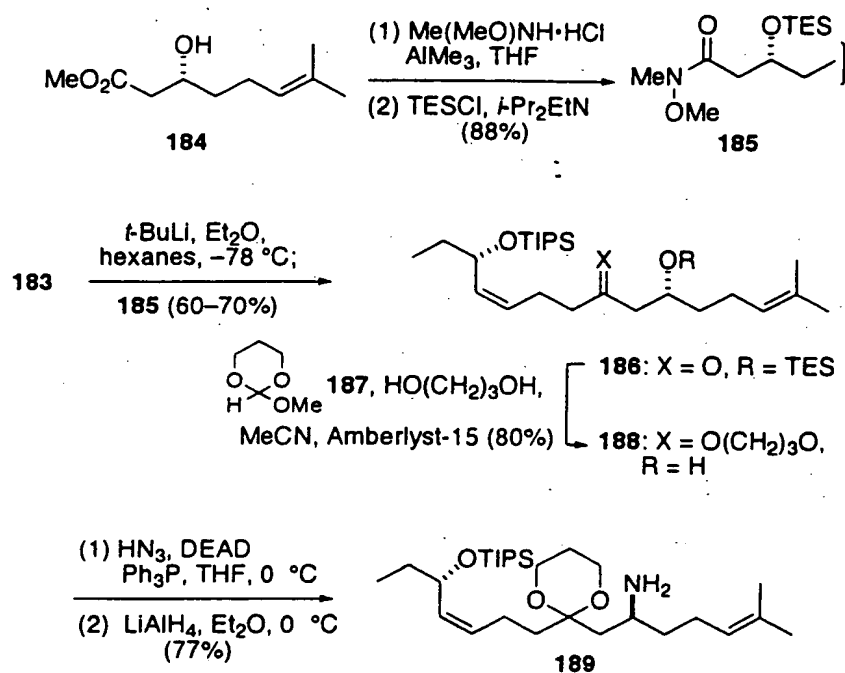


Figure 54

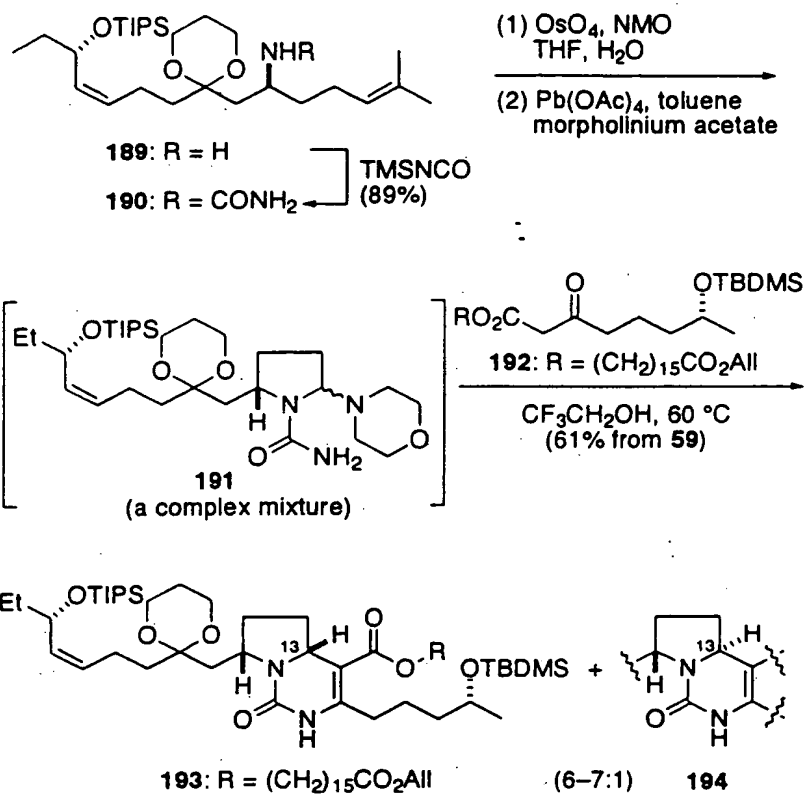


Figure 55



# National Cancer Institute Developmental Therapeutics Program

## Mean Graphs

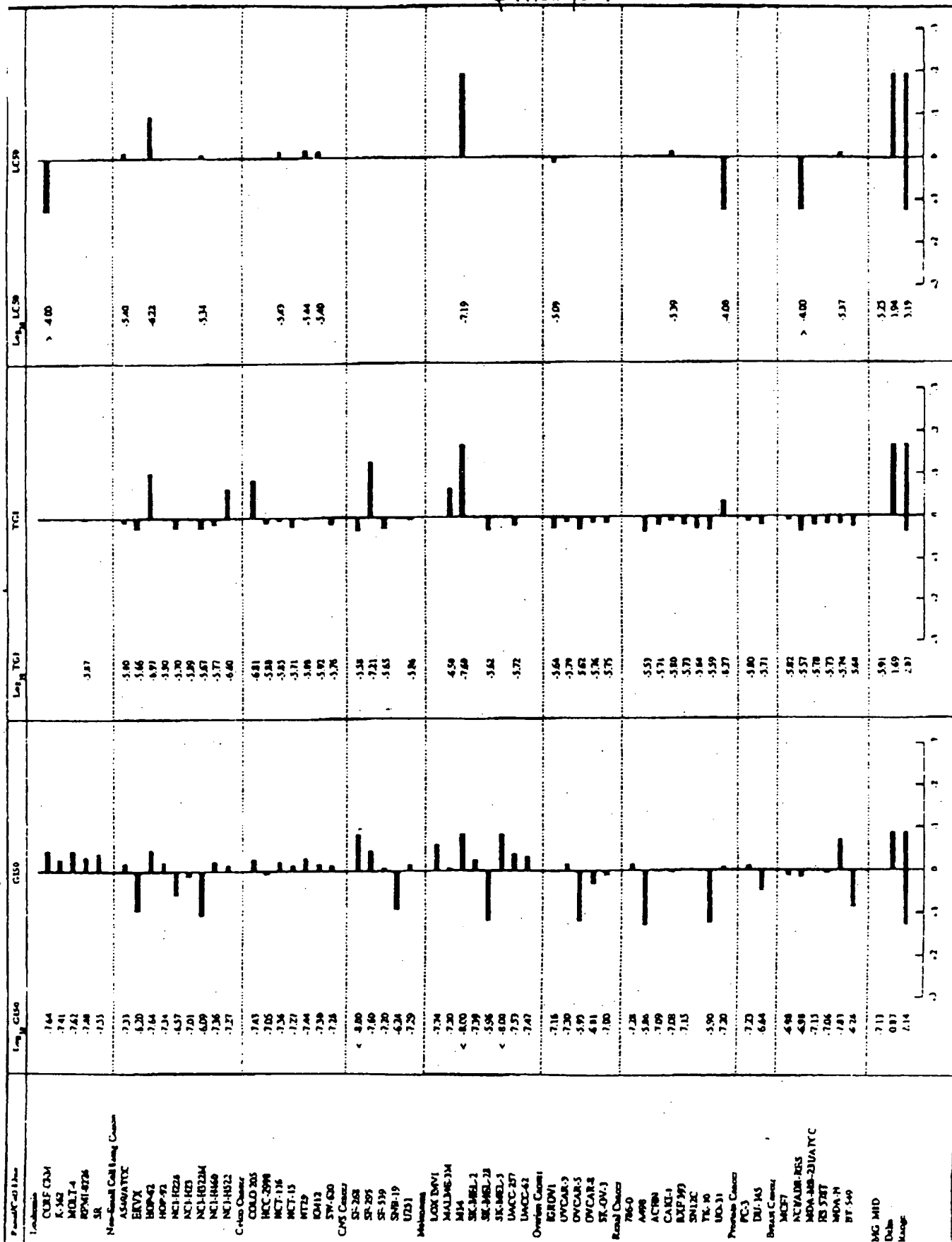
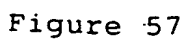
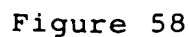


Figure 56

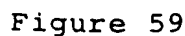
## Mean Graphs



## Mean Graphs



## Mean Graphs



Mean Graphs

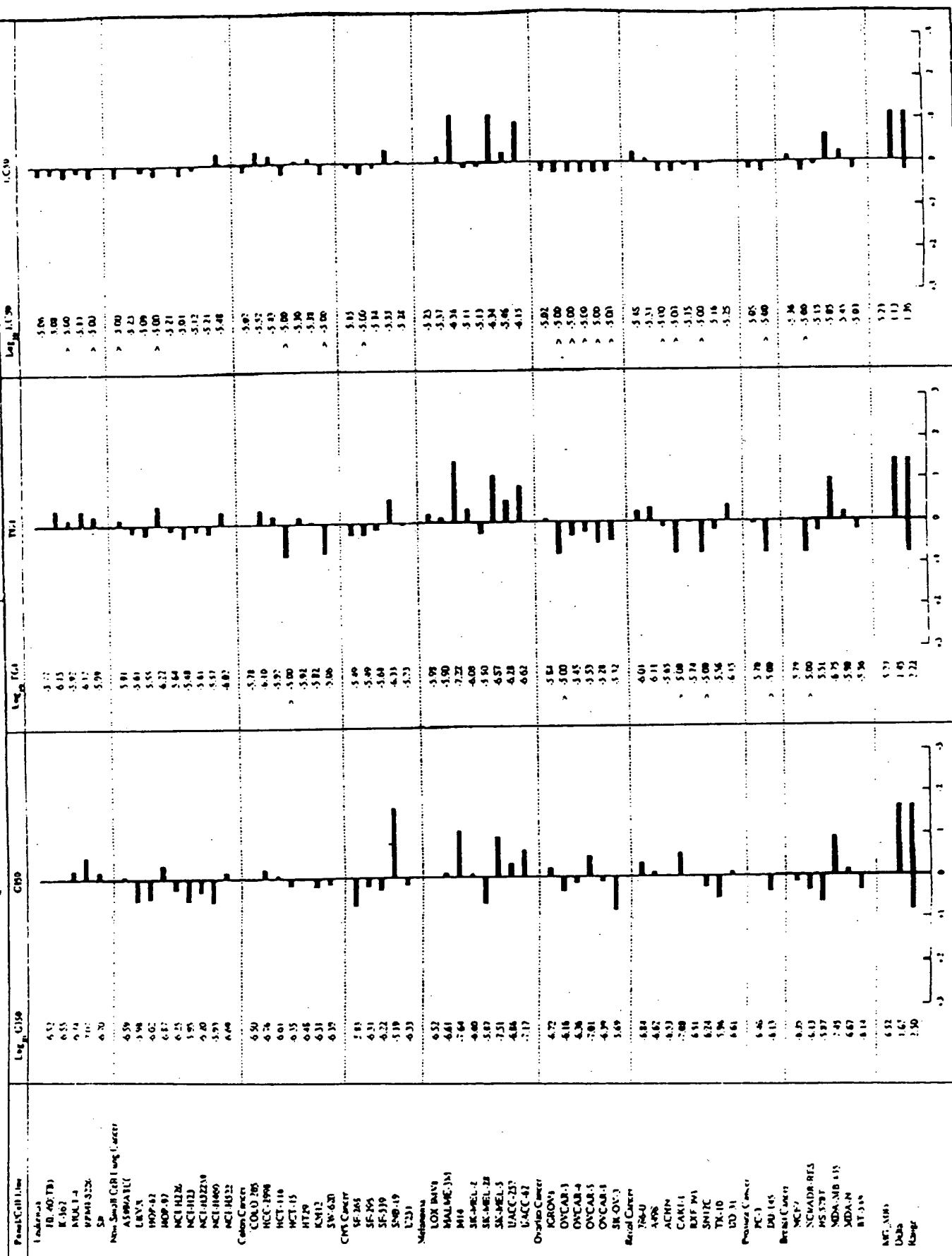
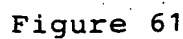


Figure 60

## Mean (Graphs)



*[Illegible handwritten text]*

